

REMARKS

The Invention

The invention features injectable polymeric compositions including a physical chemical protecting group or organic solvent and methods of their use. The polymers are capable of forming a hydrogel in situ and are useful for sustained drug delivery and to prevent postoperative adhesions.

The Office Action

Claims 1-21 are pending. Claims 1-21 stand rejected for indefiniteness. Claims 1-14 stand further rejected for obviousness over Parker et al. (U.S. Patent No. 6,218,464; hereafter "Parker) in view of Jodal et al. (Starch 1984, 36:140-143; hereafter "Jodal"). Claim 17 is rejected for obviousness over Parker in view of Jodal and Rhee et al. (U.S. Patent No. 5,324,775; hereafter "Rhee"), and Claims 15, 16, and 18-21 stand further rejected for obviousness over Harmer et al. (U.S. Patent No. 6,281,400) in view of Rhee. These rejections are addressed below.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-21 stand rejected for indefiniteness. Regarding claims 1-3 and 5-21, the Office has rejected the claims for reciting the phrase "a physical chemical protecting group that inhibits gel formation" because "said physical chemical protecting group is not defined in the claims and it is not clear how said group

inhibits gel formation.” As an initial note, claims 15, 16, and 18-21 do not recite this language, and the rejection of these claims should be withdrawn. Applicants traverse this rejection as applied to claims 1-3, 5-14, and 17, because the cited term is defined in the specification on pages 9 and 10.

Regarding the definition of claim terms M.P.E.P. § 2173.05(a) states:

During patent examination, the pending claims must be given the broadest reasonable interpretation consistent with the specification...
When the specification states the meaning that a term in the claim is intended to have, the claim is examined using that meaning...
(citations omitted, emphasis added).

Thus, the definition provided for a claim term in the specification does not need to be recited in the claims, and a rejection for indefiniteness due to the absence of such a recitation is improper.

The instant specification defines a “physical chemical protecting group” as “a group or a molecule that interacts with a hydrophobic interacting group in a manner such that the hydrophobic interacting groups are prevented from interacting with each other to an extent such that gelation occurs” (pg. 9, l. 23 – pg. 10, l. 2). The claims should be interpreted in light of this definition

Regarding the mechanism of how a physical chemical protecting group prevents gel formation, the specification provides teachings sufficient for one skilled in the art to understand the scope and meaning of the claims. Each of independent claims 1, 2, 14, and 17 requires “a polymer comprising a water soluble polymer domain with at least two hydrophobic interacting groups attached

thereto, wherein said hydrophobic interacting groups bind strongly to each other in an interchain manner to form a hydrogel under physiological conditions.” Thus, a fundamental property of a polymer of the instant claims is that it spontaneously forms a hydrogel in aqueous solution by interchain interactions between hydrophobic groups, i.e., the hydrophobic groups on one polymer molecule interact strongly with the hydrophobic groups of other polymer molecules, and the cumulative effect of the many interactions between polymer molecules is gel formation. The basic function of a physical chemical protecting group is to physically interact with a hydrophobic interacting group so that it is unavailable to interact with other hydrophobic groups. A physical chemical protecting group, as defined above, is any molecule or group that prevents enough of the interchain interactions between polymer molecules to prevent hydrogel formation. The physical chemical protecting group may prevent the interchain interaction by a variety of mechanisms, and the specification, on page 16, gives several examples of such mechanisms. In one example, a physical chemical protecting group is a molecule, such as cyclodextrin, that partially encapsulates a hydrophobic interacting group to prevent any physical interaction between the interacting group and other hydrophobic interacting groups. In another example, a bulky hydrophilic group is bound to the polymer proximal to the hydrophobic interacting group, and this bulky group provides a physical barrier to interactions between hydrophobic interacting groups. In any event, one skilled in the art reading the

specification and the claims would understand what it is that Applicants claim. As stated in M.P.E.P. § 2173.05(a), the claims must be interpreted in view of the specification; given the teachings of the specification regarding the mechanism of action of physical chemical protecting groups, the rejection for indefiniteness should be withdrawn.

Regarding claims 2, 13, 14, and 17, the Office has rejected the claims for reciting the phrase “a molecule that disrupts an interaction between said physical chemical protecting group and said hydrophobic interacting groups” because “said molecule and said physical chemical protecting group are not defined in the claims and it is not clear how said molecule disrupts the interaction.” The rejection of a “physical chemical protecting group” is discussed above. Regarding “a molecule that disrupts an interaction between said physical chemical protecting group and said hydrophobic interacting groups,” Applicants respectfully traverse this rejection.

The term “molecule” is well known in the art and does not need to be defined in the claims. Furthermore, the specification defines “disrupts,” “physical chemical protecting group,” and “hydrophobic interacting group,” and, as discussed above, the claims must be read in light of these definitions.

Furthermore, the specification teaches mechanisms of the disruption of the interaction of physical chemical protecting groups with hydrophobic groups. As discussed above, a physical chemical protecting group prevents gel formation by

preventing the physical interaction between hydrophobic interacting groups. The disruption of the interaction between a physical chemical protecting group and hydrophobic interacting groups therefore allows gel formation. A molecule that disrupts this interaction removes the physical chemical protecting groups from the vicinity of the hydrophobic interacting groups, allowing the hydrophobic interacting groups to bind to one another. The particular mechanism by which a given molecule disrupts the interaction between the protecting group and the interacting group depends on the nature of the physical chemical protecting group, but determination of the means by which the protecting group can be rendered ineffective is a straightforward matter for a chemist. The specification gives several examples of such disrupting molecules. In Example 5, the molecule is an enzyme that degrades the physical chemical protecting group. In Example 6, the molecule is a small molecule that binds the physical chemical protecting group more strongly than the hydrophobic interacting group, thereby competitively inhibiting the interaction between the physical chemical protecting group and the hydrophobic group. Since the specification explains the function of the molecules required in the instant claims and gives specific examples of mechanisms of action, one skilled in the art would understand the scope and meaning of claims 2, 13, 14, and 17. Accordingly, this aspect of the rejection for indefiniteness should be withdrawn.

In response to the rejection of claims 4 and 9 for confusion over the definition of “protecting group,” Applicants have amended claim 4 to recite a physical chemical protecting group. The rejection may now be withdrawn.

Rejections under 35 U.S.C. § 103(a)

Claims 1-14 stand rejected for obviousness over Parker in view of Jodal, and claim 17 stands rejected for obviousness over Parker in view of Jodal and Rhee. Applicants note that the teachings of Jodal appear to be relevant only to claims 2, 13, 14, and 17.

The legal standard for obviousness is recited in M.P.E.P. § 2142, which states:

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant’s disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991).

This standard has not been met in the present case. The references do not teach or suggest all of the claim limitations, nor is there a motivation to combine the references to arrive at the claimed invention.

Independent claims 1, 2, 14, and 17 recite hydrogel or hydrogel precursor compositions including “a polymer comprising a water soluble polymer domain with at least two hydrophobic interacting groups attached thereto” (emphasis added). In contrast, Parker is directed to the synthesis of random copolymers of fluorinated and water-soluble monomers. Since the polymerization of Parker is random, i.e., the monomers are dispersed randomly throughout the polymer rather than in distinct domains, the polymers of Parker do not contain a water soluble domain, as required by instant claims 1-14 and 17. Moreover, Parker is directed to the synthesis of random copolymers that include less than or equal to 10% of a highly water-soluble non-fluorinated monomer. Thus, the copolymer is mostly hydrophobic, as would be usually desired in a fluoropolymer. Indeed, Parker teaches that their compositions may be used to increase water repellency when applied to surfaces (col. 5, ll. 49-61). Since the hydrophobic compositions of Parker repel water, they are thus not hydrogels or hydrogel precursors, i.e., compositions that absorb water, as required by the instant claims. Jodal does not remedy the deficiencies of Parker as it merely describes the kinetics and products of the enzymatic degradation of cyclodextrin and says nothing regarding water-soluble polymer domains.

In addition, regarding claims 2, 13, 14, and 17, there is no motivation to combine Parker with Jodal. As stated in M.P.E.P. § 2143.01, “[t]he mere fact that references can be combined or modified does not render the resultant combination

obvious unless the prior art also suggests the desirability of the combination” (citations omitted; emphasis in original). Parker is directed to the formation of emulsion polymers using cyclodextrin, but it is silent regarding the removal of the cyclodextrin. In addition, unlike the present invention, Parker is not directed to a controlled transition of a polymer from a liquid to a gelled state under physiological conditions. The reference does not teach or suggest that removal of the cyclodextrin is necessary, or even desirable. While Jodal teaches that enzymatic degradation of cyclodextrin is possible, it is silent with regard to any specific application for such degradation, much less the application of cyclodextrin degradation in the area of polymer chemistry. Absent motivation, this ground for the rejection should be withdrawn.

Claim 17 is directed to a method of incorporating a sensitive biological material into a hydrogel of the invention by combining the composition of claim 1 with a sensitive biological material and then employing a disrupting molecule to initiate gelation. As stated above, Parker and Jodal fail to teach the limitations of claim 1. While Rhee teaches the formation of gels including biological materials, such as growth factors, such gels are formed by covalent bonding and not by the interchain interaction between hydrophobic groups, as required by claim 17. Thus, the teachings of Rhee do not remedy the deficiencies of Parker and Jodal, and this aspect of the rejection should be withdrawn.

Claims 15, 16, and 18-21 stand rejected for obviousness over Harmer in view of Rhee. Applicants traverse this rejection.

The Office states:

Harmer et al. provides a process comprising preparing a liquid composition of a fluorinated polymer and removing the organic solvent by techniques known in the art... Harmer et al. teaches that gelation of the composition occurs only after removal of the organic solvent.

This statement is incorrect. The polymers of Harmer are water-soluble and do not form gels upon removal of any organic solvents. Specifically, Harmer teaches:

The highly fluorinated ion-exchange polymers are used within the context of the present invention in a liquid composition form (also called a solution) which can be ... modified as needed to remove a portion of the water, alcohols or any volatile organic by-products by distillation or other methods known in the art to give a liquid composition consisting essentially of the water and the polymer. (col. 4, l. 62 – col. 5, l. 4; emphasis added)

Thus, Harmer teaches a liquid form of fluorinated polymers, which is a liquid when in contact with organic solvents and remains a liquid even after removal of any organic solvents. The only gelation referred to by Harmer is that of inorganic silicate and not the fluorinated polymer (col. 6, l. 36 – col. 7, l. 34).

Rejected independent claims 15, 16, and 18 each recite, in part, a polymer capable of forming a hydrogel in the absence of an organic solvent. As stated above, the polymers of Harmer do not form a hydrogel in the presence or absence of an organic solvent. Thus, Harmer does not teach the polymers recited in claims 15, 16, and 18. In addition, as stated above, while Harmer does discuss gelation, it

does so only with regard to inorganic silica, which is irrelevant to the patentability of the instant claims. Rhee teaches gel formation of a polymer upon contact with tissues and the incorporation of biological materials, such as growth factors. Rhee says nothing about a polymer that can form a hydrogel upon removal of an organic solvent and thus fails to cure the defects of Harmer as applied to claims 15, 16, and 18.

Based on the foregoing reasons, the rejection of claims 1-14 over Parker and Jodal, the rejection of claim 17 over Parker, Jodal, and Rhee, and the rejection of claims 15, 16, and 18-21 over Harmer and Rhee should be withdrawn.

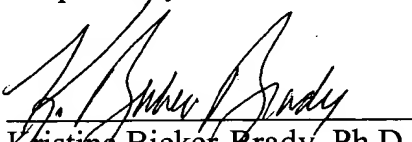
CONCLUSION

Applicants submit that the claims are now in condition for allowance, and such action is respectfully requested. Enclosed is a petition to extend the period for replying for three months, to and including July 10, 2003. If there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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